

RECEIVED
CENTRAL FAX CENTER Docket No. BB-138
2 NOV 03 2006 Serial No. 10/528,630

In the Claims

This listing of claims will replace all prior versions and listings of claims in this application.

1 (Currently amended). A polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24~~ SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide.

2 (Original). The polynucleotide of claim 1 which is DNA, genomic DNA or RNA.

3 (Currently amended). A vector comprising a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24~~ SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;

- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide.

4 (Original). The vector of claim 3 in which the polynucleotide is operatively linked to expression control sequences allowing expression in prokaryotic and/or eukaryotic host cells.

5 (Currently amended). A host cell genetically engineered to comprise a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOS 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24~~ SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a

polypeptide having bitter substance binding activity;
or the complementary strand of such a polynucleotide.

6 (Withdrawn). A transgenic non-human animal comprising a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24;
- (b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide.

7 (Currently amended). A process for producing a polypeptide encoded by a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24~~ SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide

of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide;

wherein said process comprises culturing a host cell comprising said polynucleotide and recovering the polypeptide encoded by said polynucleotide.

8 (Cancelled).

9 (Currently amended). A polypeptide having the amino acid sequence encoded by a polynucleotide selected from the group consisting of:

(a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24~~ SEQ ID NO: 2;

(b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a

polypeptide having bitter substance binding activity;
or the complementary strand of such a polynucleotide; or that is obtainable by culturing a host cell comprising said polynucleotide and recovering the polypeptide encoded by said polynucleotide

10 (Withdrawn). An antibody that specifically binds to a polypeptide having the amino acid sequence encoded by a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24;
- (b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide; or that is obtainable by culturing a host cell comprising said polynucleotide and recovering the polypeptide encoded by said polynucleotide

11 (Currently amended). A nucleic acid molecule which specifically hybridizes to a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24~~ SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOs: 1, 3, 5, 7~~,

~~9, 11, 13, 15, 17, 19, 21, and 23~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;

- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;
or the complementary strand of such a polynucleotide.

12 (Currently amended). An antagonist/inhibitor against a polypeptide having the amino acid sequence encoded by a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24~~ SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide;
or that is obtainable by culturing a host cell comprising said polynucleotide and recovering the polypeptide encoded by said polynucleotide;
wherein said antagonist/inhibitor is an antibody, the extracellular domain of said polypeptide or a fragment thereof, or an inhibiting RNA.

13 (Withdrawn). The antagonist/inhibitor of claim 12, wherein said inhibiting RNA is, RNAi, siRNA, a ribozyme, or an antisense construct hybridizing to a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24;
- (b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide.

14 (Currently amended). A process for isolating a compound that binds to a polypeptide encoded by a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32,~~

~~34, 36, 38, 40, 42, 44, 46, 48 and 50 SEQ ID NO: 2;~~

(b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

wherein said process comprises:

- (1) contacting said polypeptide, or a host cell genetically engineered with said polynucleotide or with a vector containing said polynucleotide, with a compound;
- (2) detecting the presence of the compound which binds to said polypeptide; and
- (3) determining whether the compound binds said polypeptide.

15 (Currently amended). A process for isolating an antagonist of the bitter taste receptor activity of the polypeptide encoded by a polynucleotide selected from the group consisting of:

(a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NO to the at 6, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48 and 50~~ SEQ ID NO: 2;

(b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are

conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter taste receptor activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter taste receptor activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter taste receptor activity;

wherein said process comprises:

(1) contacting said polypeptide, or a host cell genetically engineered with said polynucleotide or with a vector containing said polynucleotide, with a potential antagonist;

(2) determining whether the potential antagonist antagonizes the bitter taste receptor activity of said polypeptide.

16 (Original). The process of claim 15 further comprising the contacting of the polypeptide with an agonist of the respective bitter taste receptor activity.

17 (Original). The process of claim 16 in which said contacting with an agonist is carried out prior, concomitantly or after step (1) of claim 15.

18 (Currently amended). The process of claim 16 in which said polypeptide and said agonist are selected from the group consisting of:

(a) the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 1 and SEQ ID NO: 2 and the agonist selected from the group consisting of acetylthiourea, N,N-dimethylthioformamide, N,N'-diphenylthiourea, N-ethylthiourea, 2-imidazolidinethione, 4(6)-methyl-2-thiouracil, N-methylthiourea, phenylthiocarbamid, 6-phenyl-2-thiouracil, 6-propyl-2-thiouracil, tetramethylthiourea, thioacetamide, thioacetanilide, 2-thiobarbituric acid, and 2-thiouracil and functional derivatives thereof;

(b) the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 9 and SEQ ID NO: 10 and the agonist selected from the group consisting of saccharin and acesulfame

~~K and functional derivatives thereof;~~

(e) ~~the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 11 and SEQ ID NO: 12 and the agonist selected from the group consisting of saccharin and acesulfame K and functional derivatives thereof;~~

(d) ~~the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 13 and SEQ ID NO: 14 and the agonist selected from the group consisting of absinthine and functional derivatives thereof;~~

(e) ~~the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 15 and SEQ ID NO: 16 and the agonist selected from the group consisting of absinthine and functional derivatives thereof;~~

(f) ~~the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 19 and SEQ ID NO: 20 and the agonist selected from the group consisting of absinthine and functional derivatives thereof;~~

(g) ~~the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 37 and SEQ ID NO: 38 and the agonist selected from the group consisting of strychnine, brucine, denatonium benzoate, and absinthine and functional derivatives thereof;~~

(h) ~~the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 41 and SEQ ID NO: 42 and the agonist selected from the group consisting of tyrosine, in particular L-tyrosine, leucine, phenylalanine, histidine, tryptophan and functional derivatives thereof; and~~

(i) ~~the polypeptide encoded by the polynucleotide of claim 1 as determined by SEQ ID NO: 43 and SEQ ID NO: 44 and the agonist selected from the group consisting of naphthyl- β -D-glucoside, phenyl- β -D-glucoside, salicin, helicin, arbutin, 2-nitrophenyl- β -D-glucoside, 4-nitrophenyl- β -D-glucoside, methyl- β -D-glucoside, esculin, 4-nitrophenyl- β -D-thioglucoside, 4-nitrophenyl- β -D-mannoside, and amygdalin and functional derivatives thereof.~~

19 (Currently amended). A process selected from the group consisting of:

A. a process for the production of a food or any precursor material or additive employed in the production of foodstuffs comprising the steps of either

(i) isolating a compound that binds to a polypeptide encoded by a polynucleotide selected

from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOS 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48 and 50 SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49 SEQ ID NO: 1 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

wherein said isolating step further comprises:

- (1) contacting said polypeptide, or a host cell genetically engineered with said polynucleotide or with a vector containing said polynucleotide, with a compound;
- (2) detecting the presence of the compound which binds to said polypeptide; and
- (3) determining whether the compound binds said polypeptide;

or

- (ii) isolating an antagonist of the bitter taste receptor activity of the polypeptide encoded by a polynucleotide selected from the group consisting of:
 - (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NO to the at s 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48 and 50 SEQ ID NO: 2;

(b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter taste receptor activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter taste receptor activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter taste receptor activity;

wherein said isolating step further comprises:

- (1) contacting said polypeptide, or a host cell genetically engineered with said polynucleotide or with a vector containing said polynucleotide, with a potential antagonist; and
- (2) determining whether the potential antagonist antagonizes the bitter taste receptor activity of said polypeptide;

and wherein the process further comprises the subsequent step of admixing the identified compound or antagonist with foodstuffs or any precursor material or additive employed in the production of foodstuffs; and

B. a process for the production of a nutraceutical or pharmaceutical composition comprising the steps of either

- (i) isolating a compound that binds to a polypeptide encoded by a polynucleotide selected from the group consisting of:
 - (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOS 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48 and 50~~ SEQ ID NO: 2;
 - (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15,~~

~~17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49 SEQ ID NO: 1~~ encoding at least the mature form of the polypeptide;

- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

wherein said isolating step further comprises:

- (1) contacting said polypeptide, or a host cell genetically engineered with said polynucleotide or with a vector containing said polynucleotide, with a compound;
- (2) detecting the presence of the compound which binds to said polypeptide; and
- (3) determining whether the compound binds said polypeptide;

or

- (ii) isolating an antagonist of the bitter taste receptor activity of the polypeptide encoded by a polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48 and 50~~ SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47 and 49~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter taste receptor activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter taste receptor activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter taste receptor activity;

wherein said isolating step further comprises:

(1) contacting said polypeptide, or a host cell genetically engineered with said polynucleotide or with a vector containing said polynucleotide, with a potential antagonist; and

(2) determining whether the potential antagonist antagonizes the bitter taste receptor activity of said polypeptide;

and wherein the process further comprises the subsequent step of formulating the compound or antagonist with an active agent in a pharmaceutically acceptable form.

20 (Cancelled).

21 (Withdrawn). A composition selected from the group consisting of:

(i) a foodstuff, including human and animal foodstuff, any precursor material or additive employed in the production of foodstuff comprising an antagonist/inhibitor against a polypeptide having the amino acid sequence encoded by a polynucleotide selected from the group consisting of:

(a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24;

(b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a)

to (c) and which code for a polypeptide having bitter substance binding activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide;

or that is obtainable by the process of claim 7;

wherein said antagonist/inhibitor is an antibody, the extracellular domain of the polypeptide or a fragment thereof, or an inhibiting RNA and

(ii) a nutraceutical or pharmaceutical composition comprising an antagonist/inhibitor against a polypeptide having the amino acid sequence encoded by a polynucleotide selected from the group consisting of:

(a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24;

(b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide;

or that is obtainable by the process of claim 7;

wherein said antagonist/inhibitor is an antibody, the extracellular domain of the polypeptide or a fragment thereof, or an inhibiting RNA and an active agent and optionally a pharmaceutically acceptable carrier.

22 (Cancelled).

23 (Cancelled).

24 (Currently amended). A method for treating an abnormally increased or decreased sensitivity towards a bitter substance, wherein said method comprises administering, to an individual in need of such treatment, one or more of the following:

A. A polynucleotide selected from the group consisting of:

- (a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in ~~SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24~~ SEQ ID NO: 2;
- (b) polynucleotides having the coding sequence, as shown in ~~SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23~~ SEQ ID NO: 1 encoding at least the mature form of the polypeptide;
- (c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;
- (d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and
- (e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;
or the complementary strand of such a polynucleotide;

B. An antibody that specifically binds to the polypeptide of claim 9; and

C. An antagonist/inhibitor against a polypeptide having the amino acid sequence encoded by a polynucleotide selected from the group consisting of:

(a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24;

(b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

or the complementary strand of such a polynucleotide; or that is obtainable by a process for producing a polypeptide encoded by a polynucleotide selected from the group consisting of:

(a) polynucleotides encoding at least the mature form of the polypeptide having the deduced amino acid sequence as shown in SEQ ID NOs 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, and 24;

(b) polynucleotides having the coding sequence, as shown in SEQ ID NOs: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23 encoding at least the mature form of the polypeptide;

(c) polynucleotides encoding a fragment or derivative of a polypeptide encoded by a polynucleotide of any one of (a) to (b), wherein in said derivative one or more amino acid residues are conservatively substituted compared to said polypeptide, and said fragment or derivative has bitter substance binding activity;

(d) polynucleotides which are at least 50% identical to a polynucleotide as defined in any one of (a) to (c) and which code for a polypeptide having bitter substance binding activity; and

(e) polynucleotides the complementary strand of which hybridizes, preferably under stringent conditions to a polynucleotide as defined in any one of (a) to (d) and which code for a polypeptide having bitter substance binding activity;

~~or the complementary strand of such a polynucleotide;~~
~~wherein said process comprises culturing a host cell comprising said polynucleotide and recovering~~
~~the polypeptide encoded by said polynucleotide;~~
~~wherein said antagonist/inhibitor is an antibody, the extracellular domain of the polypeptide or a~~
~~fragment thereof, or an inhibiting RNA.~~